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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,439	12/07/2000	Paul C. Anderson	950.030US2	1720

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EXAMINER

COLLINS, CYNTHIA E

ART UNIT	PAPER NUMBER
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1638

12

DATE MAILED: 09/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/732,439	ANDERSON ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Cynthia Collins	1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 19 February 2003.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 59-96 is/are pending in the application.
- 4a) Of the above claim(s) 64-71 and 74-96 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 59-63,72 and 73 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All
  - b) Some \*
  - c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
  - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ .
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>5,6</u> .	6) <input type="checkbox"/> Other: _____ .

**DETAILED ACTION**

The Amendment filed February 19, 2003, paper no.11, has been entered.

Claim 72 is newly amended.

Claims 59-96 are pending.

Claims 64-71 and 74-96 are withdrawn from consideration.

Claims 59-63 and 72-73 are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

***Information Disclosure Statement***

Initialed and dated copies of Applicant's IDS forms 1449, filed December 7, 2000 and June 1, 2001, Paper Nos. 5 and 6, are attached to the instant Office action.

***Claim Rejections - 35 USC § 112***

Claims 59-63 and 72-73 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed November 19, 2002.

Applicants' arguments filed February 19, 2003, have been fully considered but they are not persuasive.

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Applicants point out that genes encoding enzymes that can elevate the levels of proline were available at the time of filing, and point in particular to the mothbean cDNA encoding delta<sup>1</sup>-pyrroline-5-carboxylate synthase disclosed in Verma et al. in U.S. Patent 5,344,923 and the soybean cDNA encoding delta<sup>1</sup>-pyrroline-5-carboxylate synthase disclosed in Hu et al. (Proc. Natl. Acad. Sci. 1992, 89:9354-9358). Applicants argue that a person of ordinary skill in the art would have known that such genes were available at the time of Applicants' invention, and Applicants point out that a similar disclosure was deemed sufficient to describe an analogous invention related to glycine betaine in a related application that issued as U.S. Patent 6,281,411 (reply page 3).

That a person of ordinary skill in the art would have known that genes such as the mothbean and soybean cDNAs encoding delta<sup>1</sup>-pyrroline-5-carboxylate synthase were available at the time of Applicants' invention does not overcome the rejection. First, the rejected claims are not limited to the use of recombinant DNA molecules encoding plant delta<sup>1</sup>-pyrroline-5-carboxylate synthases. The rejected claims are directed to the use of recombinant DNA molecules obtained from any source and encoding any enzyme of any type which catalyzes the synthesis of the osmoprotectant proline. The disclosure in the prior art of two cDNAs obtained from plants and encoding the same proline biosynthetic enzyme is not sufficient to describe the structural features common to a genus as broad as the genus encompassing recombinant DNA molecules obtained from any source and encoding any enzyme of any type which catalyzes the synthesis of the osmoprotectant proline and which confers to a transformed monocot plant tolerance or resistance to a reduction in water availability. Second, the rejected claims require that the expressed enzyme have the effect of conferring to a transformed monocot plant tolerance

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or resistance to a reduction in water availability. Neither Verma et al. nor Hu et al. disclose such a function for the mothbean and soybean cDNAs encoding delta<sup>1</sup>-pyrroline-5-carboxylate synthase. Third, that a similar disclosure was deemed sufficient to describe an analogous invention related to glycine betaine in a related application that issued as U.S. Patent 6,281,411 is not germane to the instant rejection because each application is examined on its own merits, and because the rejected claims are not directed to the use of recombinant DNA molecules encoding glycine betaine biosynthetic enzymes.

Claims 59-63 and 72-73 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record set forth in the office action mailed November 19, 2002.

Applicants' arguments filed February 19, 2003, have been fully considered but they are not persuasive.

Applicants argue that the claims are fully enabled by the specification, and that the Examiner has put forth no evidence sufficient to doubt their enablement. Applicants argue that because their invention is not limited to a particular gene, their failure to disclose the identification or isolation of a particular gene and/or plant comprising recombinant DNA encoding an enzyme involved in proline synthesis is not relevant to the enablement of the invention. Applicants point out that they have enabled a person of ordinary skill in the art to make transgenic plants using mannitol producing enzymes in U.S. Patent No. 5,780,709, and to

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make transgenic plants using glycine betaine producing enzymes in U.S. Patent No. 6,281,411.

Applicants also point out that they have equated mannitol, glycine betaine and proline as osmoprotectants when over-expressed in transgenic plants, and further argue that the Examiner has failed to meet the burden of establishing a *prima facie* case of lack of enablement by showing any evidence that equivalence of proline with mannitol has not been established (reply pages 3-4).

Applicants additionally point out that the sequences for genes involved in proline biosynthesis were known in the art at the time of filing, and that proline has long been identified as playing a role in plants under water deficit. Applicants further point out that they have previously taught the use of increased mannitol and increased glycine betaine as a means for imparting water stress tolerance to transgenic monocot plants in U.S. Patent 5,780,709 and U.S. Patent 6,281,411, and argue that their success in using the *mtlD* gene to impart drought tolerance to a monocot plant reduces the unpredictability in the art with respect to the use of other genes that are known to function in plants. Applicants argue that the knowledge of proline accumulation in plants in response to drought stress combined with the knowledge of sequences encoding proline biosynthetic enzymes from soybean and mothbean would have enabled one skilled in the art to prepare at the time of filing transgenic plants expressing a proline biosynthesis gene, and to expect both an increase in proline and water stress tolerance in said plants (reply page 4).

The Examiner maintains that the rejected claims are not enabled. First, the failure to disclose the identity or isolation of a particular gene and/or plant comprising recombinant DNA encoding an enzyme involved in proline synthesis is highly relevant to the enablement of the

claimed invention precisely because the invention is not limited to a particular gene. The disclosure of genes encoding proline biosynthetic enzymes that are useful for conferring to a transgenic plant tolerance or resistance to a reduction in water availability provides the skilled artisan with guidance for discriminating between those genes encoding proline biosynthetic enzymes that would have such an effect and those that would not. Such guidance is necessary because the ability of a recombinant DNA encoding an enzyme involved in proline biosynthesis to confer tolerance or resistance to a reduction in water availability is unpredictable, as the ability of a proline biosynthetic enzyme to confer tolerance or resistance to a reduction in water availability would be limited by the cellular environment in which the enzyme is expressed.

Second, that Applicants have enabled a person of ordinary skill in the art to make transgenic plants using mannitol producing enzymes in U.S. Patent No. 5,780,709 and to make transgenic plants using glycine betaine producing enzymes in U.S. Patent No. 6,281,411 is not germane to the instant rejection, because each application is examined on its own merits, and because the rejected claims are not directed to the use of recombinant DNA molecules encoding mannitol producing enzymes or glycine betaine biosynthetic enzymes. Furthermore, the Examiner can find no basis for the necessity to establish a *prima facie* case of lack of enablement by showing evidence that equivalence of proline with mannitol has not been established, as the enablement rejection was not based on a lack of equivalence of proline with mannitol.

Third, the Examiner does not dispute that sequences for genes involved in proline biosynthesis were known in the art at the time of filing, or that proline has long been identified as playing a role in plants under water deficit. The Examiner maintains, however, that it would require undue experimentation for one skilled in the art to practice the claimed invention,

notwithstanding Applicants' success in using the *mtlD* gene to impart drought tolerance to a monocot plant, or the teachings of the prior art with respect to the knowledge of proline accumulation in plants in response to drought stress and the knowledge of sequences encoding proline biosynthetic enzymes from soybean and mothbean. The Examiner notes that the *mtlD* gene used to impart drought tolerance to a monocot plant encodes an enzyme involved in mannitol biosynthesis, not proline biosynthesis. It is thus unclear why the use of the *mtlD* gene to impart drought tolerance to a monocot plant is relevant to the enablement of the rejected claims, as mannitol and proline are distinct compounds that are produced by the activities of different sets of biosynthetic enzymes. The Examiner also notes that the rejected claims are not limited to genes that are known to function in plants. The rejected claims are directed to the use of recombinant DNA molecules obtained from any source and encoding any enzyme of any type which catalyzes the synthesis of the osmoprotectant proline. The Examiner maintains that the specification does not provide sufficient guidance for one skilled in the art to discriminate, without undue experimentation, between those recombinant DNA molecules that would function in plants to produce proline in amounts sufficient to confer tolerance or resistance to a reduction in water availability and those that would not.

Claims 61-63 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record set forth in the office action mailed November 19, 2002.

Applicant's arguments filed February 19, 2003, have been fully considered but they are not persuasive.

Applicant argues that the claims are not indefinite as "increased" is defined in the specification at pages 6 and 8 of the specification (reply page 5).

The rejection is maintained because the definition of "increased" in the specification at pages 6 and 8 is not interpreted as limiting "increased" in the rejected claims. The definition at page 6 is in reference to increasing the mannitol content in cells, whereas the rejected claims are directed to increasing the proline content in cells. The definition at page 8 refers to alternative definitions for "substantially increased" or "elevated" levels of an osmoprotectant in a transformed plant cell.

Claim 73 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record set forth in the office action mailed November 19, 2002.

Applicant's arguments filed February 19, 2003, have been fully considered but they are not persuasive.

Applicant argues that the amendment of claim 72 to depend from claim 64 should overcome the rejection as claim 73, which depends from claim 72, is now directed to the seed of a definite transformed monocot plant (reply page 6).

The rejection is maintained because it is still unclear what transgene the seed is transgenic for, as transgenic seed of the transformed plant of claim 72 could contain transgenes in addition to those used in the method of claim 64. Claim 73 is directed to a transgenic seed of

the transformed plant of claim 72. Claim 72 is now directed to a transformed monocot plant regenerated from transformed plant cells obtained by the method of claim 64. While the plant cells of claim 64 are transformed with DNA encoding an enzyme which catalyzes the synthesis of the osmoprotectant proline, claim 64 does not require that the plant cells be nontransgenic prior to their transformation.

***Claim Rejections - 35 USC § 102***

Claims 59-60 remain rejected under 35 U.S.C. 102(e) as being anticipated by Verma et al. (U.S. Patent No. 5,639,950, issued June 17, 1997, filed June 29, 1994, having an effective filing date of September 29, 1992), for the reasons of record set forth in the office action mailed November 19, 2002.

Applicant's arguments filed February 19, 2003, have been fully considered but they are not persuasive.

Applicant argues that Verma et al. does not anticipate the claimed invention because the instant application has an effective filing date of August 25, 1993, and because Verma et al. is effective only as of its June 1994 filing date for the disclosure of "corn". Applicant also argues that the claimed transformed monocot plants are substantially tolerant or resistant to a reduction in water availability, whereas the parent of Verma et al. (Application No. 07/953,695, filed September 29, 1992, issued September 6, 1994 as U.S. Patent No. 5,344,923) merely discloses the sequence of a recombinant DNA encoding  $\Delta^1$ -pyrroline-5-carboxylate synthetase. Applicant additionally argues that neither Verma et al. nor its parent are enabled for the transformation of monocots (reply page 6).

The Examiner maintains that Verma et al. II (U.S. Patent No. 5,639,950) has an effective filing date of September 29, 1992, because there is no substantial difference between the disclosure of Verma et al. II and the disclosure of the parent application, Verma et al. I (U.S. Patent No. 5,344,923), with respect to making and using plants transformed with a recombinant DNA encoding  $\Delta^1$ -pyrroline-5-carboxylate synthetase. The Examiner also maintains that Verma et al. I (U.S. Patent No. 5,344,923) discloses transgenic plants comprising a recombinant DNA encoding  $\Delta^1$ -pyrroline-5-carboxylate synthetase (column 5 first full paragraph and Table I), and that such plants would inherently be substantially tolerant or resistant to a reduction in water availability. Furthermore, Verma et al. I (U.S. Patent No. 5,344,923) teaches the use of a recombinant DNA encoding  $\Delta^1$ -pyrroline-5-carboxylate synthetase to increase proline content in transgenic plants as a means of enhancing osmotic stress tolerance (column 1 through column 2 fourth paragraph; column 5 second full paragraph). The Examiner additionally maintains that Verma et al. I is enabled for the transformation of monocots, as monocot transformation was known in the art as of the filing date of Verma et al. I.

***Claim Rejections - 35 USC § 103***

Claims 59-63 and 72-73 remain rejected under 35 U.S.C. 103(a) as being unpatentable over by Verma et al. (U.S. Patent No. 5,639,950) in view of Rayapati et al. (Plant Physiology, 1989, Vol. 91, pages 581-586) and in light of Applicant's admitted prior art, for the reasons of record set forth in the office action mailed November 19, 2002.

Applicant's arguments filed February 19, 2003, have been fully considered but they are not persuasive.

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Applicant argues that Verma et al. is not enabled for the transformation of monocots.

Applicant additionally argues that Rayapati et al. does not cure the defect of Verma et al. as Rayapati et al. is a biochemical paper that contains no teaching with respect to transgenic plants.

Applicant further argues that the combined teachings of Verma et al. and Rayapati et al. would not motivate one of ordinary skill in the art to transform corn, as the combined references do not teach fertile transformed corn (reply page 7).

The Examiner maintains that Verma et al. teach corn, wheat, barley and rye monocot plants comprising a recombinant DNA encoding  $\Delta^1$ -pyrroline-5-carboxylate synthetase which catalyzes the synthesis of the osmoprotectant proline (column 17 claim 5 and column 18 claim 14). The Examiner also maintains that Verma et al. is enabled for the transformation of monocots, as monocot transformation was known in the art as of the effective filing date of Verma et al. The Examiner finally maintains that Rayapati et al. would motivate one of ordinary skill in the art to transform a plant with a recombinant DNA encoding both a proline biosynthetic enzyme and a chloroplast transit peptide, because Rayapati et al. teach that native  $\Delta^1$ -pyrroline-5-carboxylate synthetase is localized in chloroplasts, and because DNA segments encoding amino terminal chloroplast transit peptides were known and used in the plant transformation art at the time of Applicant's invention.

### *Conclusion*

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Remarks***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC

August 29, 2003

DAVID T. FOX  
PRIMARY EXAMINER  
GROUP 180 1638

*David T. Fox*